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Commentary

Biogenic amines in foods: Histamine and food processing

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Abstract. Biogenic amines, e.g. histamine, occur in many different foods. At high concentrations, they are risk factors for food intoxication, whereas moderate levels may lead to food intolerance. Sensitive persons, with insufficient diamine oxidase activity, suffer from numerous undesirable reactions after intake of histamine containing foods. Besides spoiled foodstuffs, especially fermented foods tend to contain elevated levels of biogenic amines, although their concentrations vary extensively not only between different food varieties but also within the varieties themselves. High histamine content in foods and beverages result from microbial contamination. The evidence of enteral histaminosis represents a challenge for the food industry to produce foods with histamine levels as low as possible. We therefore investigated critical steps for histamine formation during food production processes, and established production methods that include low-histamine technology.

Key words: Histamine – Biogenic amines – Food – Intolerance – Wholesomeness

Introduction

Biogenic amines are organic, basic nitrogenous compounds of low molecular weight, usually formed by decarboxylation of free amino acids: Removal of the alpha-carboxyl group from a proteinogenous amino acid leads to the corresponding biogenic amine. The names of many biogenic amines correspond to the names of their originating amino acids: Histamine from histidine, tyramine from tyrosine, beta-phenylethylamine from phenylalanine, tryptamine from tryptophane [1]. In addition to their well known occurance and important role as endogenous regulators of several human physiological processes, biogenic amines occur in many different foods and beverages, although their concentrations vary extensively not only between different food varieties but also within the varieties themselves [1, 2]. In spite of being considered as endogenous to certain foods, such as some fruits and vegetables, biogenic amines in foods normally are formed as a result of non-controled microbial action [3].

Foods likely to contain elevated levels of biogenic amines include fish and fish products, dairy products, meat and meat products, fermented vegetables and soy products, and alcoholic beverages such as wine and beer [4]. The most important biogenic amines occuring in foods and beverages are histamine, beta-phenylethylamine, tyramine, tryptamine, putrescine, cadaverine, spermine and spermidine.

Normally, during the food intake process in the human gut, low amounts of biogenic amines are metabolized to physiologically less active degradation products. This detoxification system includes specific enzymes (e.g. diamine oxidase DAO). However, upon intake of high loads of biogenic amines with foods, this detoxification system is unable to eliminate biogenic amines sufficiently. Moreover, in case of insufficient DAO-activity, caused by e.g. genetic predisposition, gastrointestinal diseases, or inhibition of DAO-activity due to secondary effects of medicines or alcohol, already low amounts of biogenic amines cannot be metabolized efficiently. If detoxification is inefficient, biogenic amines are readily absorbed and get into systemic circulation, leading to toxic effects [5–11]. Besides DAO, monoamine oxidases (MAO) distributed in different tissues of the human body also participate in the physiological inactivation of biogenic amines. Again, certain drugs (MAO-inhibitors) are well known to decrease the activity of MAO, leading to an increased risk for pathophysiological processes after intake of food contaminated with biogenic amines.

It has been known for some time that, due to the very effective pharmacological properties of biogenic amines, uptake of biogenic amines from foods and beverages can have profound effects on human health and well-being. Whereas high histamine consumption causes life threatening intoxication, lower amounts can lead to headache, nausea, hot flushes, skin rashes, sweating, respiratory distress, cardiac and intestinal problems [2, 12, 13]. Therefore, biogenic amines are of concern in relation to food spoilage, food safety, and food intolerance, and their content in foods should

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be as low as possible. The most frequent foodborne intoxications and intolerances, caused by biogenic amines, involve histamine. The evidence of histamine-related food intoxication [2, 4], histamine-induced food intolerance [10, 11, 13] and enteral histaminosis [6, 9] clearly represents a challenge for the food industry to produce foods with extremely low histamine levels. About twenty years ago, Biodyn started a special research and development programme entitled "healthy and modern nutrition", of which low-histamine technology was one of its focal points.

Low-histamine technology

Histamine never has a favorable effect on foodstuffs, on the contrary, histamine diminishes their quality. The level of histamine content in foods and beverages is a good indication of the quality of these foodstuffs. Fresh and properly stored or processed foods and beverages have low histamine contents. Within the same food variety, products with lower histamine content are clearly of better quality, since histamine can cause symptoms of food intolerance or even food poisoning [4, 9, 11].

Pre-requisites for the undesired formation of biogenic amines, such as histamine, by microorganisms in foods are availability of free amino acids, presence of decarboxylase-active microorganisms, and favorable conditions for decarboxylation of amino acids.

Free amino acids either occur as such in foods, or may be liberated through proteolysis. Normally, the presence and composition of free amino acids in a certain foodstuff cannot be changed without major changes of its taste, flavour and nutritional value. Therefore, state of the art technology must focus on complete lack of unwanted, decarboxylase-active microorganisms, and/or use of process conditions that do not allow amino acid decarboxylases to be active. Production of foods and beverages, practically free of histamine, is an important element of good manufacturing practice in food technology.

Milk and dairy products are good examples to demonstrate the undesired increase of histamine content during non-proper food processing (Table 1).

Whereas fresh milk normally contains very low levels of histamine, commercially available pasteurized or UHT milk already shows slightly higher histamine content. Upon fermentation of milk, a considerable increase of histamine content often occurs, leading to contents of up to 7 ppm histamine in sour cream and even slightly higher levels in yoghurt. Finally, in cheese production a rather drastic increase of histamine content often occurs, leading to maximum levels of histamine of up to 2500 ppm in aged cheese.

Table 1. Histamine content in milk and dairy products. Increase of histamine content during processing of milk to distinct dairy products.

Product	Histamine content (ppm)
Fresh milk	< 0.3
Pasteurized milk	0.3–0.7
UHT milk	up to 0.8
Sweet or sour cream	up to 7.0
Yoghurt	up to 13
Cheese	up to 2500

A similar situation is found during wine production: Fresh grape juice has a neglectibly low histamine content of less than 0.01 ppm, whereas some wines were found to contain up to 20 ppm of histamine!

Thus, the key question for food technology is: How this unwanted increase of histamine content can be avoided without changing sensoric and nutritional quality aspects of the foodstuffs? Since histamine does not at all influence organoleptic characteristics of foods, its unwanted presence – even in relatively high concentrations – or its absence does not influence taste or flavour.

Numerous bacteria and some yeasts are reported to express histidine decarboxylase activity, thus having the capacity to form histamine [3, 14]. Among the bacteria are several species of the genera *Bacillus, Clostridium, Enterobacter, Escherichia, Lactobacillus, Pediococcus, Proteus, Pseudomonas*, and *Salmonella*. There is good evidence that in processed (fermented) foods the contaminating microflora rather than the starter cultures is responsible for the generation of increasing histamine levels [15]. Nevertheless, in microbial food processing, all starter culture candidates (e.g. strains of *Lactobacillus*) should also be carefully checked for their potential of histamine formation, under the appropiate processing conditions, and only strains with no or low histamine formation capacity should be selected for production purposes. Microbial strains with high proteolytic enzyme activity also potentially increase the risk for histamine formation in food systems, by increasing the availability of free histidine.

Evidently, foods or raw materials rich in free histidine, such as some fish species (scombroid fish, herring, and anchovies) are potentially more jeopardized to contain high histamine levels. Moreover, the level of free histidine in fish and fishery products even increases during storage, due to the action of endogenous and contaminating proteases. Therefore, in order to keep histamine levels in fish and fish products as low as possible, both proteolytic and decarboxylation activities must be inhibited immediately after the catch. Several studies clearly show that immediate storage on ice drastically decreases the rate of histamine formation, although not completely inhibiting it.

In general, results from numerous investigations demonstrate that high histamine contents in most foods and beverages mainly result from microbiological contamination, while other biogenic amines may also derive from starter culture activities. Since biogenic amines may exert synergistic effects and compete for detoxification by DAO, food producers should optimize their technology to guarantee low levels for all biogenic amines in their products.

Beer and wine are known to contain many different biogenic amines in various amounts and compositions. So far more than twenty different biogenic amines have been detected in wine, among more than sixhundred other wine components (Table 2). Predomonant biogenic amines in wine are histamine, tyramine, putrescine, isopentylamine and β-phenylethylamine. In wines from different european origin maximum levels were recently reported as high as 16.6 mg/l for histamine, 20.2 mg/l for tyramine, and 76 mg/l for putrescine [16]. Mean levels of histamine were at 3.63 mg/l for french wines, 2.19 mg/l for italian wines, and 5.02 mg/l for

Table 2. Biogenic amines in wine.

Butylamine	Indole	Piperidine
Cadaverine	Isopropylamine	Propylamine
1,3-Diaminopropane	Isopentylamine	Pyrrolidine
Dimethylamine	Methylamine	2-Pyrrolidone
Ethanolamine	2-Methylbutylamine	Putrescine
Ethylamine	Morpholine	Serotonine
Hexylamine	Pentylamine	Spermidine
Histamine	β-Phenylethylamine	Spermine
		Tyramine

spanish wines [16]. Histamine and other biogenic amines can easily be determined by reversed-phase HPLC [16, 17].

Since alcohol is known to impair DAO-activity, extremely low levels of histamine and other biogenic amines in alcoholic beverages are of crucial importance and of special interest to the consumer [18–21].

For the generation of high quality wine and sparkling wine, Biodyn and partners have developed two methods that include low-histamine technology: Methode Schlumberger and Método Estévez. The two methods were aimed at bringing the art of wine and sparkling wine production to utmost perfection. Both Schlumberger (Austria) and Estévez (Spain) were the first wineries in their countries with recognized DIN EN ISO 9002 quality management systems. In order to identify risks and hazards during production and storage of foods, which could lead to reduced quality of the products or even be harmful for the consumers, a specific control system is needed: HACCP concept. *H*azard-*A*nalysis- and *C*ritical-*C*ontrol-*P*oint systems are best qualified as a strategy for improvement of good quality. HACCP system comprises several steps: Execute hazard analysis, determine critical control points and critical limits, building up a monitoring system, determine corrective actions, establishement of verification criteria and documentation. HACCP system may be part of a DIN EN ISO 9000 Quality Management System.

As mentioned, fresh and good quality grape juice has a very low, almost neglectable histamine content, but wine derived from this grape juice can have a considerable, unacceptable histamine content. Therefore, we applied HACCP concept to the multistep process of wine production, with special focus on the histamine formation.

Sparkling wine: Methode Schlumberger

For production of sparkling wine by traditional method (Méthode Champenoise), high risk of histamine formation occurs at first and second alcoholic fermentation, as well as at malolactic fermentation. Medium risk is at storage between first and second fermentation, before filtration.

Although the prefermentation steps such as vintage, pressing and must clarification normally represent only a low risk for histamine formation, excessive pressing and inadequate must clarification not only lead to poorer quality of must but also to an increased potential for formation of histamine. The result of inclusion of low histamine technology in 1983 into Methode Schlumberger (see http://www.schlumberger.co.at) is seen in Figure 1.

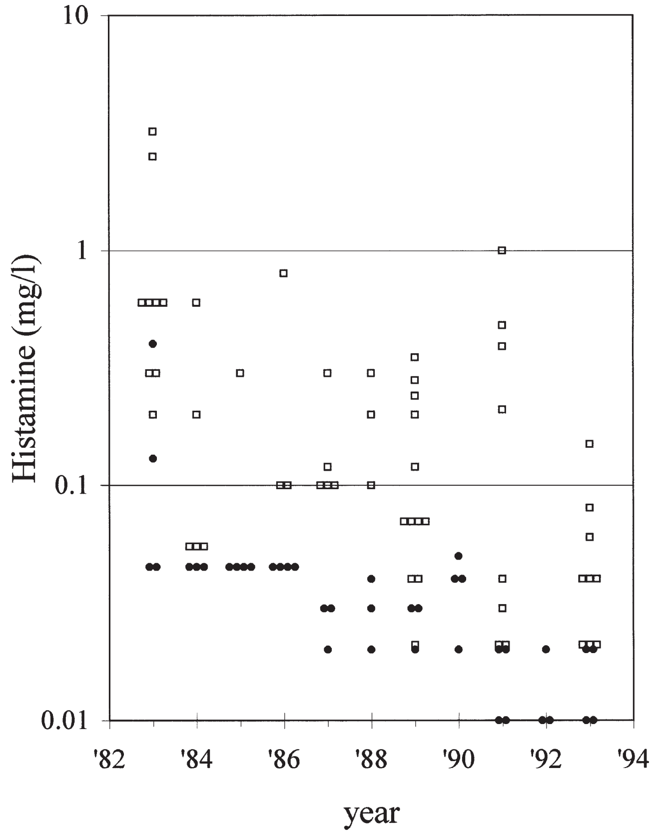

Fig. 1. Histamine levels in austrian sparkling wines. Ninety-four different samples were purchased between 1983 to 1993 from the local market and analysed for histamine content. ● Schlumberger, □ other austrian sparkling wines.

A recent study in 1995 confirmed that sparkling wines, generated by Methode Schlumberger, always contain extremely low levels of histamine when compaired to other sparkling wines of the same provenance (Figure 2).

Sherry wine: Método Estévez

The traditional method for elaboration of sherry is the solera system developed in southern Spain: Young wine is sequentially added to older wine in proportion to the amount of older wine removed. Fractional blending is conducted periodically in all stages (criaderas) in a system of piled up oak casks [22]. In 1992, Biodyn started a collaborative project with the sherry bodega Marqués del Real Tesoro, José Estévez S. A., in Jerez, Spain. The goal was to improve the quality of sherry, and application of low-histamine technology to the traditional way of sherry production was the first step. Application of HACCP concept to the multistep production scheme of sherry, with regard to the risk of histamine formation, demonstrated that the most critical steps for unwanted histamine formation during the generation of sherry are alcoholic fermentation, and ageing of young sherry wine in the traditional solera system, respectively. Crucial are also storage before solera and blending after the solera system, latter because a single sample from a histamine containing cask can spoil a whole production lot.

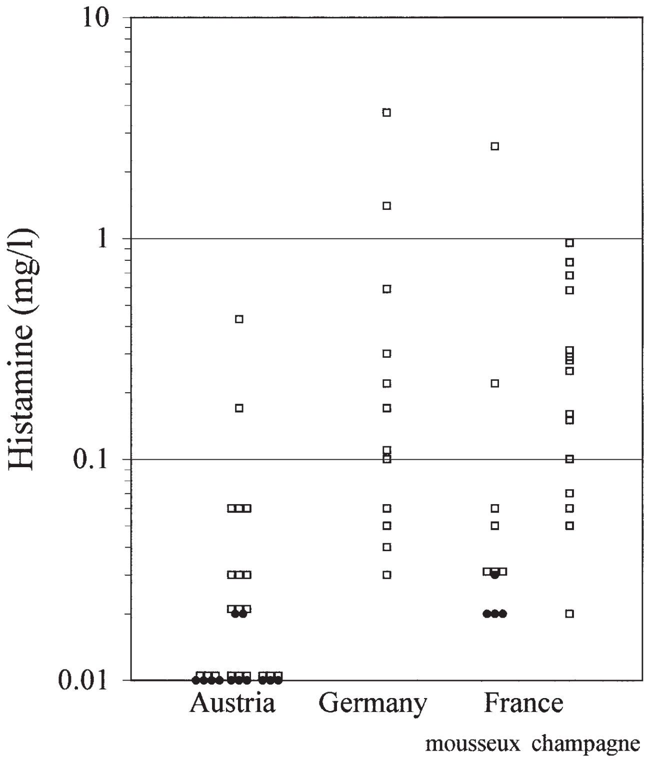

Fig. 2. Histamine levels in sparkling wines from Austria, Germany and France. Comparison of Methode Schlumberger to conventional traditional method. Seventy different samples were purchased in 1995 from the local market and analysed for histamine content. ● Methode Schlumberger, □ conventional traditional method.

Comparable to the situation with sparkling wine, vintage and pressing represent a rather low risk.

Analysis of more than fifty sherry samples from the Jerez sherry-producing zone, taken from the local market, demonstrates that the vast majority of these samples contains rather high amounts of histamine, with maximum levels of more than 10 mg/l.

Only one sample can be regarded as practically histamine-free, as a result of application of inclusion of low histamine technology into Método Estévez: TIO MATEO with a histamine content of less than 0.02 mg/l, corresponding to up to 500 times less histamine than some of the other sherry samples (Fig. 3).

Taken together, application of low histamine technology to the traditional methods for production of sparkling wine or sherry allows elaboration of sparkling wines (Methode Schlumberger) or sherry wines (Método Estévez) of premium quality and practically free of histamine.

Conclusions

Histamine never has a favorable effect on our foods and beverages, on the contrary, histamine diminishes their quality. Histamine does not affect organoleptic characteristics, but clearly does induce food intolerance in an increasing number of human population. Therefore, histamine content – and content of other harmful biogenic amines – must be limited to the lowest possible level.

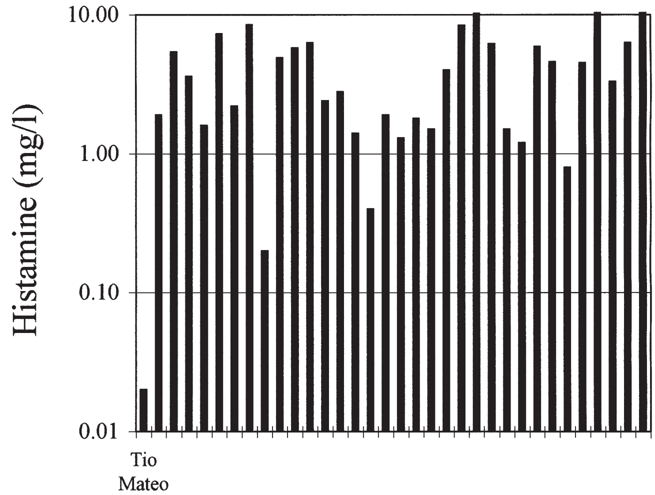

Fig. 3. Histamine levels in Sherry wines from the Jerez region. Thirty-four different samples were purchased in 1995 from the local market and analysed for histamine content.

Although every food variety requires special precautions and technology (HACCP concept), there are a few common parameters which can be defined for low-histamine technology.

First, high quality raw materials, free of histamine, must be used. Additionally, proper and careful treatment (harvest, transport, storage) of raw materials until processing is absolutely necessary. Growth and activity of decarboxylase-positive microorganisms (spoilage microbes) must be avoided, and activity of endogenous proteases and amino acid decarboxylases have to be inhibited. This can be achieved by technological measures (removal of endogenous microflora) and proper and hygienic production conditions (cooling, freezing, salting etc.) If microbial transformations such as alcoholic or other fermentations are part of the production process, use of specifically selected starter cultures for these fermentations is important, as well as strict control of the whole fermentation process. Activity of foodborne decarboxylases and unwanted microbial activity must be suppressed, while fermentation is performed under strict control by selected, decarboxylase negative starter cultures. Finally, the whole production process should be embedded in a specific quality system, such as DIN EN ISO 9000 quality management system, including analytical control at critical points.

In view of the well documented health hazards caused by histamine and other harmful biogenic amines in foods [9–11], consumers who may be at risk should have the possibility to actively select low-histamine products from the shelves. Full information for the consumer and the protection from health hazards are key aspects of food legislation. Therefore, food varieties with a potential to contain harmful amounts of histamine, e.g. wine and beer, should be specifically labeled with regard to their histamine content. This would provide consumers with essential information as regards the nature of the product, and increase consumer safety by allowing him to make an informed choice concerning the puchase of foods. That is why Biodyn has created a special label enabling direct identification of products essentially

free of histamine. The label shows the trade-mark of Biodyn AG, a cristal in a hexagon, and also contains interesting information on histamine related food intolerance.

As demonstrated here, production of premium quality foodstuffs with extremely low levels of histamine is possible. Therefore, low-histamine technology must be applied to more products.

Practically histamine-free, premium quality products not only are of major importance to all modern consumers, but also allow the growing number of individuals at risk a more diversified nutrition. Even though histamine induced food intolerance causes major impairment of life quality to an increasing part of our population, most cases remain undiagnosed or misdiagnosed [10]. Therefore, there is an absolute need for better information of physicians, dieticians and consumers.

Finally, stricter legal regulation have to be adapted. So far, only few countries have defect or hazard action levels for histamine in their food regulation, mostly restricted to fish, and these levels do not yet consider the evidence from enteral histaminosis. In the interest of the consumers, better and more severe regulations are needed, also for wine and beer, and they should be harmonized among the different nations.

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